OLFACTORY-LIKE RESPONSES IN PYRIFORM AREA TO NON-OLFACTORY STIMULATION[*]

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Considerable doubt continues to exist about the rôle of finely myelinated and unmyelinated[†] visceral afferents in the function of the cerebral cortex. Recent evoked potential studies involving stimulation of the chorda tympani,[20,21] the vagus,[6,7,14] and the splanchnic nerves[3] have failed to establish that impulses transmitted along the *slow-conducting*[‡] components of these nerves reach the cortex. It is inferred, however, from clinical evidence that the slowly conducted signals are discriminated at the cortical level.

The inability to resolve the foregoing problem by the usual physiological techniques indicated the need for other methods. For this reason it was decided to re-explore the bioelectrical properties of the olfactory system in the hope of gaining a clue to the physiology of visceral systems in general. Olfaction is unique in being both an extero- and visceroceptive sense. Its anatomical substratum has attributes that make it a prototype of a primitive visceral system. The primary olfactory neurone manifests a most primitive characteristic insofar as it assumes a position in the dermal layer. The olfactory nerves going to the bulb are entirely unmyelinated. From the primary cell station in the bulb a large proportion of fibers travel in the olfactory tract directly to a phylogenetically ancient part of the cortex. In short, one has in the olfactory apparatus a system that begins with entirely unmyelinated fibers and is irrefutably known to reach the cerebral cortex.

The cortical responses in the pyriform area following natural olfactory stimulation are strikingly dissimilar to those obtained from the neocortex by natural activation of visual, auditory, or somesthetic receptors. In contrast to the latter, one finds an olfactory stimulus is followed by a sustained train of rhythmically recurring sinusoidal potentials of high voltage. Adrian, employing the hedgehog and the cat, appears to have been the first to describe such potentials as occurring in both the olfactory bulb and the pyriform cortex.[1] Figure 1 shows responses to olfactory stimulation recorded from the pyriform area in the opossum, rabbit, cat, and the squirrel

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[†] Used in the classical sense.

[‡] As opposed to the faster conducting components.

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monkey. In view of the similarity of the microanatomical organization of the pyriform cortex in all osmatic mammals,[22] the kind of responses illustrated in the figure might be expected to be found in all such forms.

The rationale for further study of the olfactory system made it particularly significant to perform the following observations: (i) to compare the type of responses obtained, respectively, by natural and by electrical stimulation; (ii) to study the effect of these two types of stimulation on the transynaptic transmission of impulses; and (iii) to ascertain to what extent various anesthetics, convulsants, autonomic drugs, etc., affect the capability of eliciting responses as well as modify their form and magnitude. In addition, one would look for the influence of other sensory systems on the bioelectrical activity of the olfactory system. During the course of initial experiments employing natural forms of stimulation, it was found that the application of sapid substances to the tongue, as well as hard pinching of various parts of the body, resulted in olfactory-like responses in the pyriform area. These responses, together with some of the significant findings in experiments employing natural olfactory stimulation, are the subject of this paper.

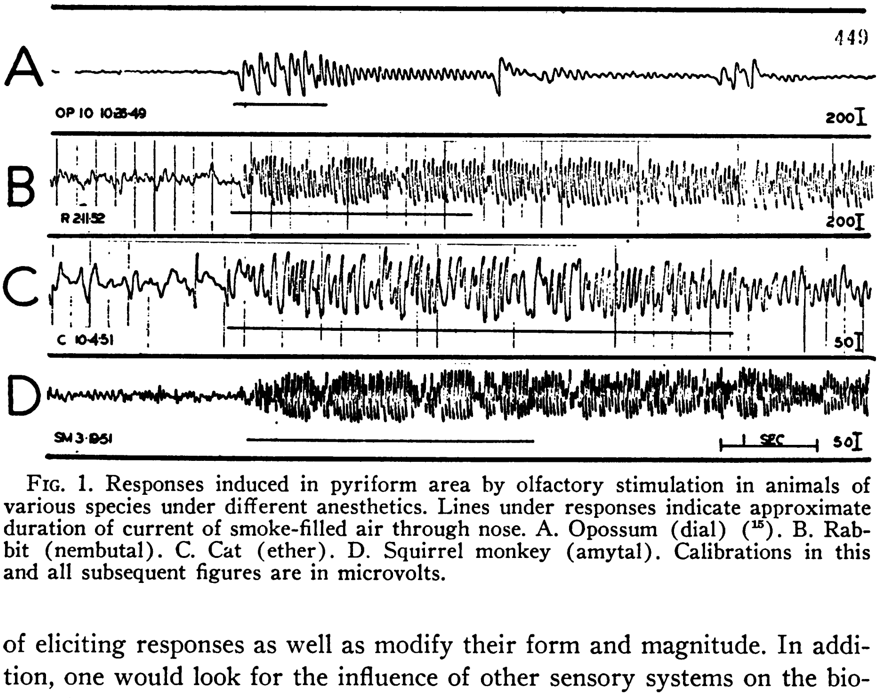

FIG. 1. Responses induced in pyriform area by olfactory stimulation in animals of various species under different anesthetics. Lines under responses indicate approximate duration of current of smoke-filled air through nose. A. Opossum (dial) ([15]). B. Rabbit (nembutal). C. Cat (ether). D. Squirrel monkey (amytal). Calibrations in this and all subsequent figures are in microvolts.

MATERIALS AND METHODS

For these preliminary experiments 30 rabbits, six cats, and two monkeys were used. Anesthetics employed to date have included ether, nembutal, dial, and amytal. In a few instances the isolated brain preparation of Bremer has been resorted to in order to avoid continued anesthesia. Gaining exposure of the pyriform area required the removal of the temporal muscles, zygoma, and the orbit. The cortex of the lateral convexity above the rhinal fissure was also exposed for the application of electrodes. As yet, the medial surface of the hemisphere has been explored in only one preparation. In those experiments requiring simultaneous examination of the pyriform area and hippocampus, the latter was usually approached through a limited exposure of the opposite hemisphere. In every instance the animal breathed through a tracheal cannula. An olfactory stimulant was delivered through a nasal catheter. In some experiments (not reported here) a variety of gases were administered at various temperatures at a rate controlled by a flow-meter. Solutions of sapid substances (salt, quinine, etc.) were usually applied to the tongue in various concentrations by means of a syringe or a cotton patty, but sometimes undissolved substances were coated on the tongue. Pinching the body wall was performed manually with a surgical clamp. Other forms of sensory stimulation, as well as experimental procedures to be dealt with more fully elsewhere, will be referred to in the appropriate context.

An eight-channel inkwriting electroencephalograph (Grass) was used because of the need to show events that were relatively slow in duration and of long temporal sequence, as well as to compare simultaneously the bioelectrical activity in several regions. The activity in two channels was also viewed on a cathode-ray oscillograph. Electrodes were of small stainless steel wire with ball tips. A reference electrode was placed on the scalp. "Monopolar" recording was used for purposes of exploring, and bipolar recording for localization. All recordings were made in a shielded room with the animal in a headholder.

Results

1. *Observations on natural olfactory stimulation.* As Adrian has emphasized,[1,2] the character of responses induced by natural olfactory stimulation will vary according to the type and depth of anesthesia. The rabbit anesthetized with nembutal provides a particularly good preparation for demonstrating olfactory responses in the pyriform area and for observing their modification during progressively lighter stages of narcosis. With intravenous nembutal this animal may pass from a very deep to a moderately light stage of anesthesia within a period of an hour. In our experience, in very deep anesthèsia (electrocorticogram practically flat) it has not been possible, as might be expected, to elicit any response. After several minutes, however, the blowing of room air into the nose will result in the appearance of a train of rhythmically recurring potentials rising abruptly from a relatively smooth base line. This is illustrated by the top recording in Figure 2 where there is a three-second train of potentials that recur quite rhythmically at about 12 per second. Thereafter, as anesthesia becomes less deep, an induced train of such potentials does not dissipate into a relatively smooth base line, but leaves in its wake a continuous background of random activity of the kind seen at the beginning of line 2 in Figure 2, and which possibly corresponds to what Adrian has termed the "intrinsic activity" in the olfactory bulb.[2] It was as though the stimulus had the effect of arousing the animal out of the deep stage of anesthesia. This random activity, which becomes more prominent in the change from moderately deep to moderately light anesthesia, may at times have intermixed with it potentials that almost have the regularity and amplitude of olfactory-induced responses.

As the animal passes from moderately deep to moderately light anesthesia, it is apparent that the frequency of the induced potentials becomes somewhat faster. This is illustrated in lines 2 and 3 in Figure 2 which shows a recording after the animal mentioned above went into the interim stage. The train begins with potentials having a frequency of about 15 per second, and, as the response continues to outlast the duration of the stimulus, the frequency slows to about 13 per second. As the animal becomes still lighter, one may expect to find induced potentials with frequencies around 20 per second. Intense forms of stimulation such as smoke (which it must be remembered is a trigeminal as well as a powerful olfactory stimulant) may be accompanied by a train of still faster, rhythmically recurring potentials lasting, with sustained voltage, for many seconds after the administration of the stimulus.

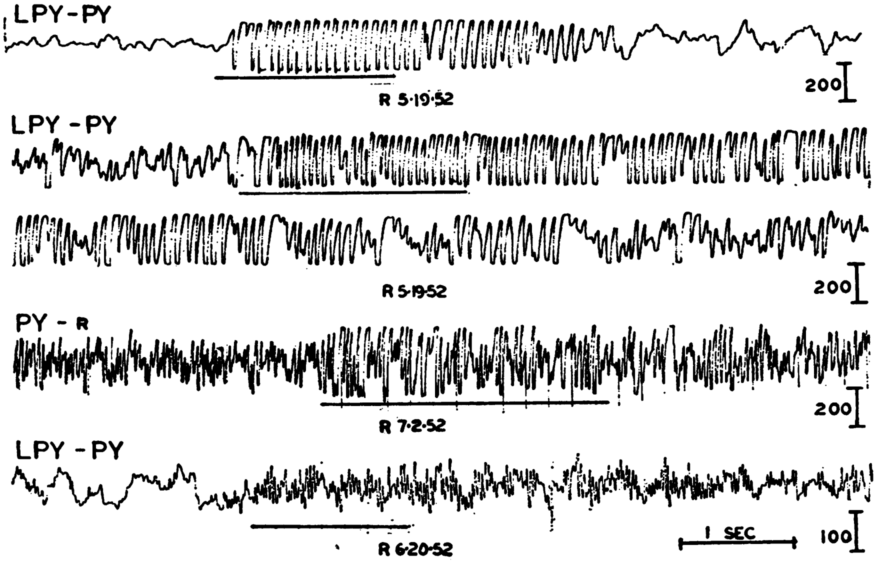

FIG. 2. Samples of responses to olfactory stimulation in pyriform area of rabbit as they appear at various stages from deep anesthesia to wakefulness. Lines under recordings indicate approximate duration of flow of room air through ipsilateral nostril. First line: response in deep nembutal anesthesia. Second line and its continuation in the third: response in the same rabbit typifying the activity seen during the period when animals of this species pass over from deep into moderately light nembutal anesthesia. Fourth line: response in moderately light nembutal anesthesia. Note how the induced potentials are obscured by the spontaneous activity. Fifth line: response in a Bremer preparation after the animal wakened from anesthesia. All samples, except the third, obtained by bipolar recording.

In line 4 of Figure 2 it is seen that by the time an animal has passed into a moderately light stage of anesthesia the spontaneous activity of the pyriform area is so fast and of such great amplitude that it is difficult to demonstrate the presence and the character of the induced response. On the other hand, in Bremer preparations, after awakening from anesthesia has occurred, we have observed induced responses characterized by fast potentials, at around 35 per second that rise gradually above base line activity.

Our experiences to date with other forms of anesthesia have brought to light no findings that add anything significant to what has already been reported by Adrian. In summarizing the foregoing account one can say that responses induced by natural olfactory stimulation are seen in clearest detail in the period between moderately deep and moderately light anesthesia. The induced potentials show some increase in frequency as anesthesia lightens, obtaining their maximum frequency after the animal has awakened from anesthesia. In good preparations the amplitude of the responses during anesthesia commonly ranges between 400 and 500 microvolts.

The pyriform cortex is a secondary olfactory station. Localization studies in the rabbit indicate that the type of responses described can also be obtained, but with less amplitude, from the cortex (seen in a lateral exposure) just above the rhinal fissure. We have not yet explored the posterior extension of the hippocampal gyrus in these studies. As Adrian has pointed out, the response occurs predominantly ipsilateral to the stimulus.[1] From the work of MacLean and Delgado[16] it is also known that the amygdala, which is likewise a secondary olfactory station, shows similar responses.

In view of the rationale for pursuing study on the olfactory system, it was most important to ascertain whether or not natural olfactory stimulation would activate structures more than two synapses removed from the receptor organ. All evidence to date indicates that the hippocampus receives no contribution directly from the olfactory bulb. If this is correct, it would be at best a tertiary station. Figure 3 shows that instillation of smoke into the *ipsilateral* nostril will bring about synchronized activity in this structure. In *A* of Figure 3, two responses to such stimulation are shown in recordings from a cat that was lightly anesthetized with ether. The employment of natural olfactory stimulation makes it impossible to assess with any exactitude the latency of responses, but our observations gave the impression that the hippocampus responded in a less predictable manner and after a longer time than the pyriform area. In *B* of Figure 3 a response is shown in a cat on which a bilateral removal of the neocortex had been performed and which was then allowed to come out of anesthesia. With nembutal anesthesia, as illustrated in Figure 3C, trains of diphasic spikes occurring at around six per second have been observed to follow olfactory stimulation. The foregoing findings, therefore, suggest that natural olfactory stimulation will activate structures more than two synapses removed from the receptors.

2. *Observations on natural gustatory stimulation.* A number of rabbits were anesthetized by ether in an attempt to duplicate studies reporting that gustatory stimulation resulted in identifiable responses in the masticatory area.[10] No success was achieved by this method. In experiments

employing nembutal anesthesia, however, it was found that application of sapid substances to the tongue resulted in olfactory-like responses in the pyriform area provided that testing was performed at a critical level of anesthesia. If the animal was quite deep in anesthesia, one might get good olfactory responses, but not gustatory ones. On the other hand, as the animal neared a moderately light stage of anesthesia, a similar situation appeared to apply. The gustatory responses were not of as great amplitude as those induced by olfactory stimulation or of as long duration. It is possible, therefore, that the increased amount of "intrinsic activity," as the anesthesia lightened, might obscure them more readily than the olfactory-induced potentials. Lines 2 and 3 in Figure 2 illustrate the character of the electrocorticogram at about the time when one has the best success in eliciting gustatory responses.

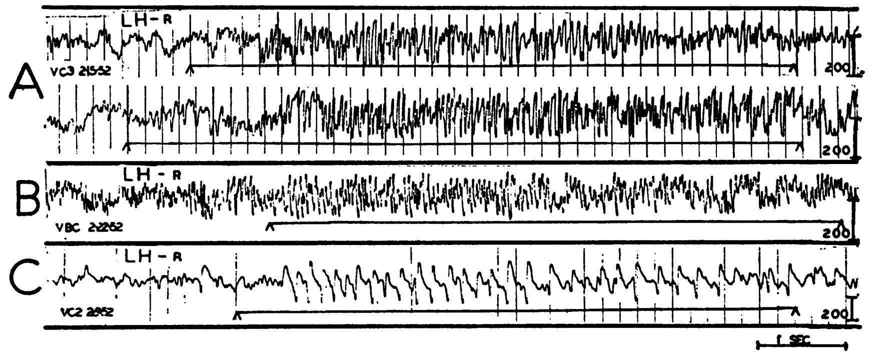

FIG. 3. Responses induced in the hippocampus by instillation of smoke through ipsilateral nostril. Lines under recordings indicate approximate time that smoke was administered. A. Two responses in cat lightly anesthetized with ether. B. Response in cat where the neopallium was removed and the animal allowed to come out of anesthesia. C. An evoked train of diphasic spikes in a cat under nembutal anesthesia. LH-R, signifies "monopolar" recording from left hippocampus.

Figure 4 gives samples of simultaneous recordings from the left pyriform cortex and the right hippocampus in the rabbit. In *A* a typical response to the instillation of room air in the left nostril is given for comparison with the gustatory responses shown in *B, C,* and *D.* In *B* a train of rather similar potentials, but of less amplitude and of shorter duration, follows in a little over two seconds the application of salt crystals to the tongue. In the time between *B* and the obtaining of the subsequent records the animal received sufficient tubocurarine to result in seizure activity of the cortex.* This

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* Tubocurarine in large doses has attributes of a convulsant drug in regard to its effect on the activity of nerve cells. Convulsant drugs were employed in a number of experiments on the supposition that they might enhance evoked responses in the pyriform area. Tubocurarine holds the advantage over convulsant drugs insofar as it assures muscular immobilization of the animal at the time it is achieving the effects of a convulsant on the cortex. This subject will be dealt with more extensively elsewhere.

activity obscured any evoked responses that might possibly have been present and it had to be abated by intravenous nembutal. After the foregoing medication the response shown in line *C* followed the application to the tongue of a cotton patty soaked in a concentrated salt solution. This was one of the two instances in the present experiments where gustatory stimulation appears to have activated the hippocampus as well. The other was in a cat (referred to above) in which the neocortex was removed and the animal allowed to come out of anesthesia. *D* is included to illustrate that the response in the pyriform area could be obtained on repeated stimulation of the tongue, although activation of the hippocampus never again became so

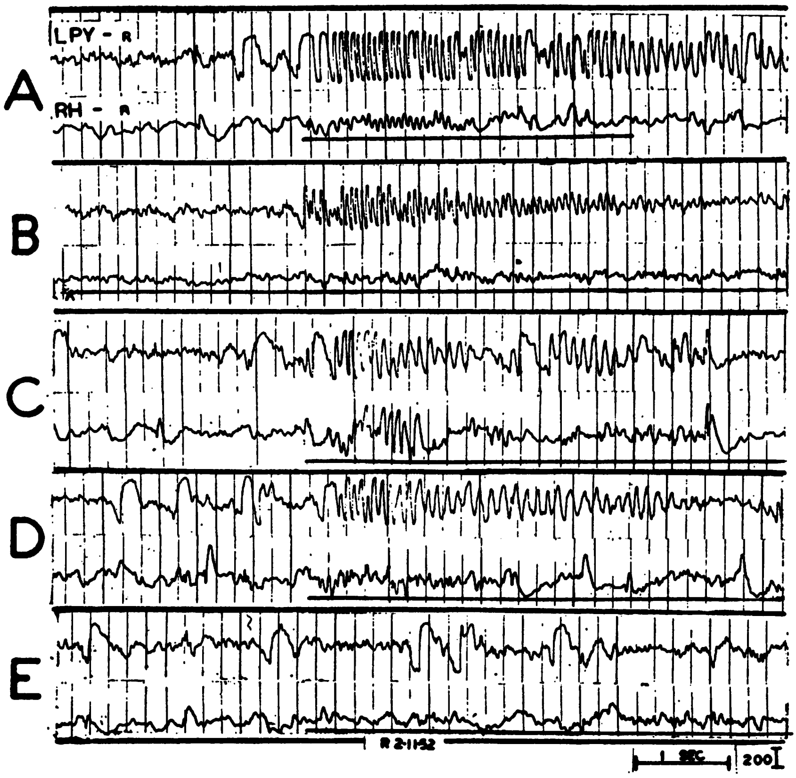

FIG. 4. Records from rabbit contrasting a typical olfactory response (A) with those obtained by gustatory stimulation (B, C, D). Moderately deep nembutal anesthesia. Simultaneous "monopolar" recording from left pyriform cortex (LPY – R) and right hippocampus (RH – R). Lines under recording from hippocampus indicate duration of the respective stimuli. In B a response follows by a little over two seconds the application of salt crystals to the tongue. C shows a response to the application to the tongue of cotton patty soaked in saline. See text for details regarding the changed experimental conditions under which this and the subsequent records were obtained, as well as for a discussion of the hippocampal activity. D, another of several responses elicited by the same procedure as in C. E, failure of response after placing a dry cotton pack in the mouth. The repeatedly negative findings following this manoeuvre indicated the above responses were not the result of touch or light pressure.

apparent as in *C*. In *E* a large pack of dry cotton was placed in the mouth without evoking any response. This manoeuvre was done in an effort to show that the evoked response did not result from pressure upon the tongue from the cotton soaked with sapid solution. The same procedure resulted in negative findings in other experiments. Other types of control will be referred to below.

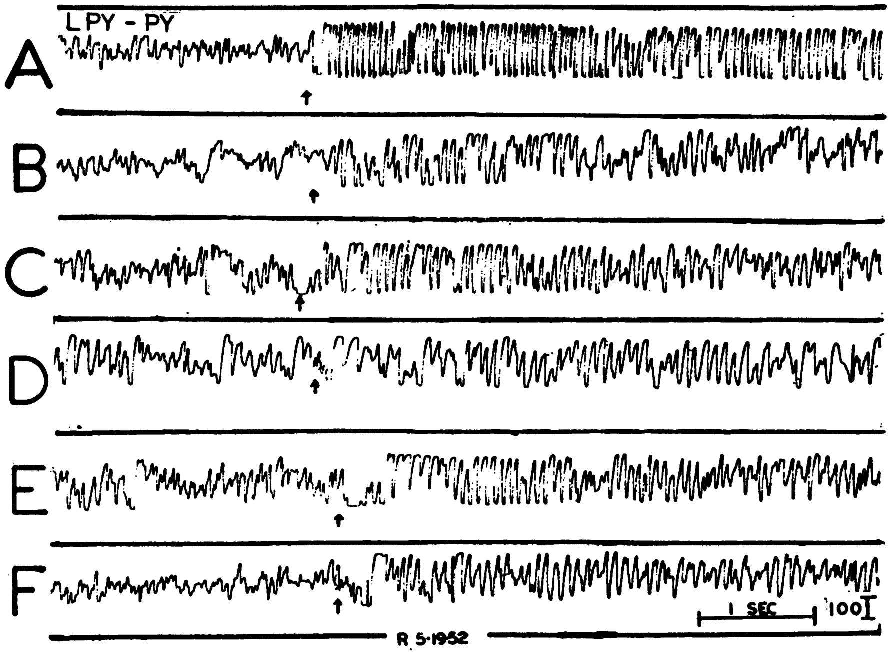

FIG. 5. Bipolar recordings from pyriform area in rabbit showing responses to gustatory stimulation and to pinching the ipsilateral ear. A typical response to olfactory stimulation is shown in A for comparison. This animal was at a somewhat lighter level of nembutal anesthesia than the one in the preceding figure. Arrows indicate application of the respective stimuli. B and C show two responses to the application of a salt patty on the tongue. The response in D resulted from syringing salt crystals off the tongue with water. E and F show similar responses obtained by pinching the tip of the ipsilateral ear. See text for results of noxious stimulation of other parts of the body.

B, C, and *D* in Figure 5 give further examples of gustatory responses in the pyriform area of a rabbit in a somewhat lighter stage of anesthesia. They may be compared with a typical response to olfactory stimulation in A. It will be noted that the gustatory responses are of lower amplitude, are less sustained, and that the frequency of the potentials is slighter slower. *B* and *C* show two responses to the application of a salt patty on the tongue, whereas in *D* the response followed a syringing with water that dissolved and spread some salt crystals that had been placed on the tongue.

Although syringing sapid solutions such as salt and quinine on the tongue resulted in responses, this method did not produce as consistent results as applying the solution by means of a cotton patty. Neither method, however, is devoid of the criticism that the responses were the result of activating other than taste receptors of the tongue. The control experiments employing dry cotton packs were partial assurance that light touch and pressure stimulation were not responsible. Showing that the response could be elicited from the anterior part of the tongue after destroying the connections of the fifth nerve would be further evidence that the potentials resulted from gustatory stimulation, although the chorda tympani also has some somesthetic fibers.[5] Attempts at bilateral removal of the Gasserian ganglion or bilateral section of the third division of the fifth nerve were unsuccessful insofar as they led to a deterioration in the quality of the electrocorticogram. Hence, negative results could not be considered conclusive. Further consideration of this problem is given in the following section.

3. *Observations on noxious stimulation.* In an effort to resolve the rôle of gustatory versus somesthetic stimulation in the activation of olfactory-like responses in the pyriform area (cf. previous section), mechanical stimulation was applied to various parts of the body. Tactile stimulation everywhere was without effect. However, if a hard pinch was applied, for example, to the ear, olfactory-like responses such as illustrated in *E* and *F* of Figure 5 were readily elicited. In this instance, the tip of the ipsilateral ear was stimulated. *F* is included to show that the response is reproducible. Similar olfactory-like responses were obtained from pinching the contralateral ear. It is seen that the responses are indistinguishable from those obtained when a gustatory stimulant was used. The same kind of responses were obtained from pinching the tongue or irritating the skin around the nostril. Clearly identifiable, but less conspicuous, responses were elicited by hard pinching of the toes of either forefoot or hindfoot. On the other hand, pinching the skin of the body did not seem to result in any perceptible change of the electrocorticogram. Hard pinching of the tail, interestingly enough, gave responses with almost as much amplitude as those obtained by stimulating regions of the face and ears. This is illustrated in Figure 7 where responses to a prolonged (A) and a short pinch of the tail (B), respectively, are compared with a typical olfactory response (Fig. 6). It is seen that a single quick pinch of the tail gives rise to almost as great and lasting a response as a sustained pinch. This calls to mind one's subjective experience on receiving a single hard pinch. In the case of the tail and extremities, as elsewhere, the surgical clamp could be put in place, and even partially closed, without any response. This indicates that touch or pressure is not sufficient to elicit the responses (at least in the anesthetized animal), but that the stimulus must be noxious. On occasion, manipulation of the tracheal cannula has resulted in olfactory-like responses in the pyriform area. Further study of the effect of noxious stimulation of the viscera is in progress.

It is to be emphasized that in the foregoing observations electrodes were placed in the frontal, insular, parietal, temporal, and occipital regions, as well as in the pyriform area. The localization of the olfactory-like responses induced by gustatory and noxious stimulation fell within the limits of that described for natural olfactory stimulation.*

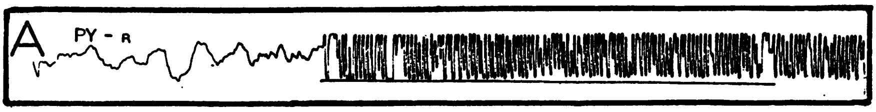

FIG. 6

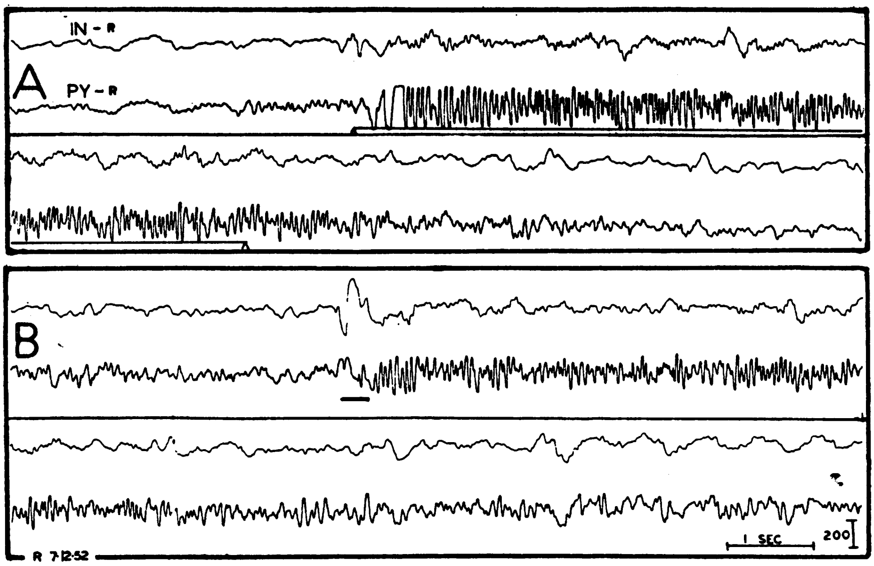

FIG. 7

FIG. 6 and FIG. 7 are recordings from the same rabbit (nembutal anesthesia). FIG. 6 shows a typical response to olfactory stimulation. It is to be compared with the activity induced by a prolonged (FIG. 7A) and brief pinch (FIG. 7B) of the tail. The latter figure shows a simultaneous "monopolar" recording from the insula (IN – R) and pyriform cortex (PY – R). Lines under recordings indicate approximate duration of the stimulus. Note that a brief hard pinch gives rise to almost as great and lasting a response as a sustained pinch.

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* The question obviously arises whether or not the responses described in the previous two sections could be the result of some fortuitous stimulation of the olfactory receptors. It has been our experience time and again that in the animal breathing through a tracheal cannula such a powerful olfactory stimulant as smoke may be enveloped around the head, and even blown into the face, without eliciting any response. This indicates that to elicit a response there must be an appreciable flow of air in the nasal passages. Furthermore, it is to be noted that these responses can be obtained in the curarized animal where the muscular paralysis insures against swallowing setting up any commotion of air in the nasopharynx.

Discussion

This paper has dealt only with observations concerning responses of the kind induced by natural olfactory stimulation. Other types of responses in the pyriform area elicited by auditory stimulation, etc., will be dealt with elsewhere. With one exception, the foregoing observations on gustatory and noxious stimulation have been obtained in the rabbit. It remains to be seen whether or not olfactory-like responses in the pyriform cortex or elsewhere can be elicited in the cat and monkey. In these latter forms, there promises to be greater difficulty in carrying out the experiments at the optimum level of anesthesia.

The pyriform area is part of the limbic cortex surrounding the hilus of the hemisphere. The hilar position of this cortex attests to its early development in phylogeny. Cytoarchitecturally, there are distinctive differences among various portions of the limbic cortex, but taken as a whole, they show similarities that make them easily distinguishable from the surrounding neopallium. In contrast to the latter, they show a relatively poor development of the layers of the outer lamina, particularly those that would correspond to the supragranular layers. In some respects the outer lamina of the limbic cortex is comparable to layer IV of the neocortex because of the distribution of the afferent plexus.[18] The limbic cortex is further distinguished from the neopallium because of its relative paucity of cells of short axis cylinder.[22] These considerations lead one to wonder whether or not activity evoked in other regions of the limbic cortex besides the pyriform area might also show similarities to the olfactory-induced responses. The posterior part of the hippocampal gyrus (angular ganglion of Cajal; entorhinal area of Brodmann) which, as Cajal pointed out,[22] has close affinities with the visual system, is the next obvious place along the limbic ring to test this possibility.

Superficially the induced, rhythmically recurring potentials in the pyriform area have some resemblance to those elicited by the cortical application of acetylcholine, suggesting the possibility of the local release of acetylcholine by nervous stimulation. This problem requires further investigation. But it may be mentioned here that in the rabbit intravenous doses of atropine large enough to lead to seizure activity of the neocortex have the effect of attenuating or even abolishing the induced rhythmic potentials and leaving in their stead a few random spikes. Convulsive drugs such as strychnine and metrazol have a similar effect.

On the other hand, the rhythmically recurring potentials may represent reverberatory activity leading to an after-discharge in closed chains of neurones. It is possible that the relative paucity of cells of short axis cylinder in the pyriform cortex,[22] and indeed the whole limbic cortex, allows reverberatory activity in self-reexciting chains of neurones to take place with greater ease than in the neopallium. It is hypothecated that these cells have a high threshold for excitation "because they generally have only a few dendrites."[12] The more of these elements, therefore, in a closed chain of neurones, the more difficulty there would be in maintaining reverberatory activity. Cajal assumed that the great number of cells with short axons in the neocortex was the anatomical expression of the delicacy of function of the human brain.[cf. 13]

The build-up and long duration of responses in the pyriform cortex following olfactory, gustatory, and noxious ("painful") stimulation suggest a lack of a delicacy of function; and one wonders if there is not manifest in this phylogenetically primitive cortex *one* of the physiological correlates of these sense modalities. All three are senses that give information regarding the intensity and quality of a stimulus, but tell little of its position in space. They are senses too that make it hard to tell subjectively when a stimulus begins and when it ceases. It is also significant to recall that the limbic cortex has recently been found to be implicated in the elaboration of emotion, and emotion is like a visceral sense insofar as it is registered in terms of quality and intensity (for further elaboration cf.[17, 18]).*

It is impossible at the present time, however, to say what significance the observations reported here have in regard to the cortical representation of taste and "pain." One cannot conclude that because stimulation of the receptors associated with these senses activates the pyriform area that the modality of these senses is represented there. Just as speculative would be the inference that these responses are a manifestation of "sensory association" or of an "alerting" or "activation" of the olfactory sense by these other senses. It will be of interest to ascertain whether or not these responses are in any way related to the function of the reticular system.

There is insufficient anatomical knowledge to designate by what route gustatory and somesthetic impressions might reach the pyriform cortex. The work of Morison, Dempsey, and Morison suggests that there may be such a pathway for the somesthetic sense through the subthalamus.[19] There are possible pathways for taste by way of the midline thalamus and the inferior thalamic peduncle, as well as other routes, according to comparative neurologists,[4] through the hypothalamus, medial forebrain bundle, etc.

Finally, it may be recalled that comparative neurologists have long claimed that the pyriform area is an olfacto-somatic correlation center. The present experiments, in addition to pointing to further electrophysiological studies, suggest the desirability of re-examining the work of Ferrier,[8, 9] Horsley and Schäfer,[11] and others in the last century that purported the limbic lobe to be concerned in the appreciation of somesthetic sensation.

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* In the light of this discussion it is also pertinent to recall that individuals with epileptogenic foci involving either the limbic or extra-limbic cortex of the fronto-temporal region are subject to a wide variety of aura that include emotional feelings, olfactory, gustatory, cardiorespiratory, and gastrointestinal sensations, and somesthetic discomforts that range from pains in the head to paresthesias in the buttocks (cf.[18]).

SUMMARY

This paper deals with the first of a series of studies on the olfactory system, the rationale for which is given in the introduction. As already known, natural olfactory stimulation results in a characteristic train of rhythmically recurring sinusoidal potentials in the pyriform area. Such responses, as might have been predicted from the similarity of the microanatomical organization of the pyriform cortex in mammals, have now been found in mammals standing low, intermediate, and high in the phylogenetic scale. The present studies have demonstrated that natural olfactory stimulation also leads to a variety of prolonged responses in the hippocampus, a structure inferred to be more than two synapses removed from the olfactory receptors.

In addition, it has been found in rabbits anesthetized with nembutal that gustatory stimulation, as well as the application of noxious stimulation to various parts of the body, leads to responses in the pyriform area that have similarities to those induced by natural olfactory stimulation. The eliciting of the olfactory-like responses appears to be critically conditioned by the level of anesthesia. Possible anatomico-physiological mechanisms responsible for the induced rhythmically recurring potentials and the implications of the present study for further research on the limbic cortex are discussed.

ADDENDUM

Since this paper went to press, one of us has had the pleasure of reviewing the foregoing material with Dr. Richard Jung of Freiburg, and Dr. Jung was reminded of rhythmic responses around 5 to 6 per second that he and Kornmüller obtained from the hippocampus and subiculum when they pinched the hindleg and other parts of the body in the unanesthetized rabbit. The reader is referred to Figure 11 of their paper, "Eine Methodik der Ableitung lokalisierter Potentialschwankungen aus subcorticalen Hirngebieten" (Arch. psychiat., 1938, *109,* 1-30).

REFERENCES

1 Adrian, E. D.: Olfactory reactions in the brain of the hedgehog. J. Physiol., 1942, *100,* 459.

2 Adrian, E. D.: The electrical activity of the mammalian olfactory bulb. EEG Clin. Neurophysiol., 1950, *2,* 377.

3 Amassian, V. E.: Fiber groups and spinal pathways of cortically represented visceral afferents. J. Neurophysiol., 1951, *14,* 445.

4 Ariëns Kappers, C. U., Huber, G. C., and Crosby, E. C.: *The evolution of the nervous system in invertebrates, vertebrates, and man.* New York, The Macmillan Co., 1936. 2 vols.

5 Costen, J. B., Clare, M. H., and Bishop, G. H.: The transmission of pain impulses via the chorda tympani nerve. Ann. Otol., Rhinol., 1951, *60,* 591.

6 Dell, P. and Olson, R.: Projections thalamiques, corticales et cérébelleuses des afférences viscérales vagales. C. rend. Soc. biol., 1951, *145,* 1084.

7 Dell, P. and Olson, R.: Projections "secondaires" mésencéphaliques, diencéphaliques et amygdaliennes des afférences viscérales vagales. C. rend. Soc. biol., 1951, *145,* 1088.

8 Ferrier, D.: XVI. The Croonian Lecture.—Experiments on the brain of monkeys. (Second series). Philos. Tr. R. Soc. London, 1875, *165,* 433.

9 Ferrier, D., and Yeo, G. F.: XIX. A record of experiments on the effects of lesions of different regions of the cerebral hemispheres. Philos. Tr. R. Soc. London, 1884, *175,* 479.

10 Gerebtzoff, M. A.: Recherches oscillographiques et anatomo-physiologiques sur les centres cortical et thalamique du goût. Arch. internat. physiol., Liége, 1941, *51,* 199.

11 Horsley, V. and Schäfer, E. A.: A record of experiments upon the functions of the cerebral cortex. Philos. Tr. R. Soc. London, 1888, *179B,* 1.

12 Lorente de Nó, R.: Studies on the structure of the cerebral cortex. I. The area entorhinalis. J. Psychol. Neur., Lpz., 1934, *45,* 381.

13 Lorente de Nó, R.: Architectonics and structure of the cerebral cortex. Chapter XV in Fulton, J. F. ***Physiology of the Nervous System.*** New York, Oxford University Press, 1949, p. 667.

14 MacLean, P. D., Pribram, K. H., and Malis, L. I.: Unpublished data.

15 MacLean, P. D. and Pribram, K. H.: Unpublished observations.

16 MacLean, P. D. and Delgado, J. M. R.: Electrical and chemical stimulation of frontotemporal portion of limbic system in the waking animal. EEG Clin. Neurophysiol. (in press).

17 MacLean P. D.: Psychosomatic disease and the "visceral brain." Recent developments bearing on the Papez theory of emotion. Psychosomat. M., 1949, *11,* 338.

18 MacLean, P. D.: Some psychiatric implications of physiological studies on frontotemporal portion of limbic system (visceral brain). EEG Clin. Neurophysiol., 1952, *4,* 407.

19 Morison, R. S., Dempsey, E. W., and Morison, B. R.: Cortical responses from electrical stimulation of the brain stem. Am. J. Physiol., 1941, *131,* 732.

20 Patton, H. D.: Physiology of smell and taste. Ann. Rev. Physiol., 1950, *12,* 469.

21 Patton, H. D. and Amassian, V. E.: Cortical projection zone of chorda tympani nerve in cat. J. Neurophysiol., 1952, *15,* 245.

22 Ramón y Cajal, S.: ***Studien über die Hirnrinde des Menschen.*** (tr. from the Spanish by J. Bresler), Leipzig, J. A. Barth, 1903, Vol. 4.